PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 341.030WO1 .	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US2004/031912	International filing date *(day/month/year)* 29/09/2004	(Earliest) Priority Date *(day/month/year)* 03/10/2003
Applicant PROMEGA CORPORATION		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 16 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
      ☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
   b. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.
2. ☐ **Certain claims were found unsearchable** (See Box II).
3. ☒ **Unity of invention is lacking** (see Box III).
4. With regard to the **title,**
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established by this Authority to read as follows:
5. With regard to the **abstract,**
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. 8
      ☐ as suggested by the applicant.
      ☐ as selected by this Authority, because the applicant failed to suggest a figure.
      ☒ as selected by this Authority, because this figure better characterizes the invention.
   b. ☐ none of the figures is to be published with the abstract.

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

   a. type of material

      ☒ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☒ in written format

      ☒ in computer readable form

   c. time of filing/furnishing

      ☒ contained in the international application as filed

      ☒ filed together with the international application in computer readable form

      ☐ furnished subsequently to this Authority for the purpose of search

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-26, 28-35, 36 partially, 40

A method for the directional subcloning of DNA fragments comprising: a) providing a first vector comprising a first selectable marker gene and a DNA sequence of interest, which DNA sequence of interest is flanked by at least two restriction enzyme sites (REs), wherein at least one of the flanking RE sites is a site for a first RE which has infrequent restriction sites in cDNAs or open reading frames from at least one species and generates complementary single-strand DNA overhangs, wherein at least one of the flanking RE sites is for a second RE which has infrequent restriction sites in cDNAs or ORFs from at least one species and generates ends that are not complementary to the overhangs generated by the first RE, wherein digestion of the first vector with the first RE and the second RE site generates a first linear DNA fragment which lacks the first selectable marker gene but comprises the DNA sequence of interest; b) providing a second vector comprising a second selectable marker gene which is distinguishable from the first selectable marker gene and non-essential DNA sequences, which non-essential sequences are flanked by at least two restriction enzymes sites, wherein at least one of the flanking RE sites in the second vector is for a third RE which generates complementary single-strand DNA overhangs that are complementary to the single-strand DNA overhang generated by the first restriction enzyme in the first linear DNA fragment, wherein at least one of the flanking RE sites in the second vector is for a fourth RE which generates ends that are not complementary to the ends generated by the first or third RE but can be ligated to the ends generated by the second RE, and wherein digestion of the second vector with the third RE and the fourth RE generates a second linear DNA fragment which lacks non-essential DNA sequences but comprises the second selectable marker, which second linear DNA fragment is flanked by ends which permit the oriented joining of the first linear DNA fragment to the second linear DNA fragment; and c) combining the first and second vectors, the first vector and the second linear DNA fragment, or the second vector and the first linear DNA fragment in a suitable buffer with one or more REs under conditions effective to result in digestion to yield a mixture comprising the first and second linear DNA molecules which are joined in an oriented manner. said method wherein at least one hapaxoterministic RE is used;

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2. claim: 27

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A method for producing a vector suitable for expression of an amino acid sequence of interest, comprising: combining at least two vectors in a suitable buffer with one or more restriction enzymes and optionally DNA ligase under conditions effective to result in digestion and optionally ligation to yield a mixture optionally comprising a third vector, wherein a first vector comprises a first selectable marker gene and a DNA sequence of interest, which DNA sequence of interest is flanked by at least two restriction enzyme sites, wherein two or more of the flanking restriction enzyme sites are sites for a first restriction enzyme which is a hapaxoterministic restriction enzyme, wherein digestion of the first vector with the first restriction enzyme generates a first linear DNA fragment which lacks the first selectable marker gene but comprises the DNA sequence of interest and a first pair non-self complementary single-strand DNA overhangs, wherein a second vector comprises a second selectable marker gene which is distinguishable from the first selectable marker gene and non-essential DNA sequences that optionally include a counterselectable gene, which non-essential DNA sequences are flanked by two or more restriction enzyme sites, wherein two or more of the flanking sites in the second vector are for a second restriction enzyme which is a hapaxoterministic restriction enzyme, wherein digestion of the second vector with the second restriction enzyme generates a second linear DNA fragment which lacks non-essential DNA sequences but comprises the second selectable marker gene and a second pair of non-self complementary single-strand DNA overhangs, wherein each of the second pair of the non-self-complementary DNA overhangs is complementary to only one of the single-strand DNA overhangs of the first pair of non-self complementary single-strand DNA overhangs and permits the oriented joining of the first linear DNA fragment to the second linear DNA fragment.

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3. claims: 37-38

A method of inducing expression of a DNA sequence of interest in a host cell, comprising contacting a recombinant host cell which is deficient in rhamnose catabolism, and has a recombinant DNA molecule comprising a rhamnose-inducible promoter operably linked to an open reading frame for a heterologous RNA polymerase, with rhamnose and an expression vector comprising a promoter for the heterologous RNA polymerase operably linked to a DNA sequence of interest.

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4. claim: 39

A method comprising introducing a vector comprising a nucleic acid fragment encoding a barnase which lacks a secretory domain into a recombinant host cell which expresses barstar from a promoter which is constitutively expressed in procaryotic cells.

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5. claims: 41-43

A vector comprising an open reading frame 3' to a DNA fragment of no more than 30 base pairs, which DNA fragment comprise a ribosome binding site, a SgfI recognition site, and a sequence which, when present in mRNA enhances the binding of the mRNA to the small subunit of a eucaryotic ribosome; a vector comprising a SgfI recognition site, a sequence which comprises ATG and which sequence when present in mRNA, enhances the binding of the mRNA to the small subunit of a eucaryotic ribosome, and an open reading frame which begins at the ATG in the sequence;

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6. claims: 44-102, (116-119,121-126,128) partially

A vector comprising a SgfI recognition site 5' to a recognition site for a first restriction enzyme which generates blunt ends; a vector comprising a first open reading frame which includes a SgfI recognition site and a recognition site which is not in the open reading frame for a restriction enzyme that has infrequent restriction sites in cDNAs or open reading frames from at least one species and generates blunt ends; a vector comprising a ribosome binding site which optionally overlaps by one nucleotide with a SgfI recognition site and a recognition site which is not in the open reading frame for a restriction enzyme that has infrequent restriction sites in cDNAs or open reading frames from at least one species and generates blunt ends; a vector comprising a first open reading frame which includes a recognition site for a first restriction enzyme that generates a 3' TA overhang and a recognition site for a second restriction enzyme that is not in the open reading frame generates blunt ends; a support comprising a plurality of recombinant vectors; a process to prepare said support; a library of recombinant cells comprising said recombinant vectors;

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7. claims: 103-114, (116-119,121-126) partially

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A vector comprising a first open frame which includes a PmeI recognition site and is linked at the 5' end by a recognition site for a first restriction enzyme that generates complementary single-strand DNA overhangs; a support comprising a plurality of recombinant vectors, wherein at least one recombinant vector was prepared by using said vector including said PmeI site; a method to prepare said support; a library of recombinant cells comprising said recombinant vectors;

8. claims: 115,120,127 (121-126,128) partially,129,130

A support comprising a plurality of recombinant vectors, two or more of which comprise an open reading frame for a different polypeptide, wherein at least one recombinant vector comprises a promoter and an open reading frame which is flanked by two exchange site; a method to prepare said support; a library of recombinant cells comprising recombinant vectors or a library of recombinant vectors comprise an open reading frame for a different polypeptide; a method to prepare a plurality of mutagenized recombinant vectors: comprising providing DNAs comprising a plurality of mutagenized open reading frames flanked by two restriction enzyme sites for a first restriction enzyme which is a hapaxoterministic restriction enzyme and generates a first pair of non-self complementary single-stranded DNA overhangs; a library of recombinant cells or a library of recombinant vectors, a plurality of which recombinant vectors comprise said mutagenized recombinant vectors;

9. claims: 131-141

A method for performing genetic analysis, comprising a) populating a database of genetic data with a plurality of genetic records; b) querying the database of genetic data to identify a first subset of genetic records; wherein each record has at least one recognition site for one predetermined restriction enzyme or for a restriction enzymes included in a set of predetermined restriction enzymes; and c) determining a set of statistics associated with the restriction enzyme recognition sites for at least a second subset of genetic records in the first subset; A computerized system for genetic analysis, comprising a database of genetic data; a processor; a set of one or more programs executed by the processor causing the processor to: query the database of genetic data to identify a first subset of genetic records; wherein each record has at least one recognition site for one predetermined restriction enzyme or for restriction enzymes included in a set of predetermined restriction enzymes, and; determine a set of statistics associated with the restriction enzyme recognition sites for at least a second subset of genetic records in the first subset;

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A. CLASSIFICATION OF SUBJECT MATTER
C12N15/10 C12N15/64 C12N15/66 C12N15/70 C12N9/22
G06F19/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C12N G06F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CAB Data, Sequence Search, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	AEBI M ET AL: "Sequence requirements for splicing of higher eukaryotic nuclear pre-mRNA." CELL. 21 NOV 1986, vol. 47, no. 4, 21 November 1986 (1986-11-21), pages 555-565, XP008052167 ISSN: 0092-8674	1-5, 14-18,26
Y	page 563, right-hand column, paragraph 2 ----- -/--	1-3,14

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search 11 November 2005	Date of mailing of the international search report 29. 11. 2005
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Authorized officer Hornig, H

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	ZELENETZ A D ET AL: "DIRECTIONAL CLONING OF CDNA USING A SELECTABLE SFII CASSETTE" GENE, ELSEVIER BIOMEDICAL PRESS. AMSTERDAM, NL, vol. 89, no. 1, 1990, pages 123-127, XP001019191 ISSN: 0378-1119	14,73, 86,87, 101,102, 120-126, 129,130
Y	abstract	88-97, 99,100
X	HAN J H ET AL: "LAMBDAGT22S, A PHAGE EXPRESSION VECTOR FOR THE DIRECTIONAL CLONING OF CDNA BY THE USE OF A SINGLE RESTRICTION ENZYME SFII" NUCLEIC ACIDS RESEARCH, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 16, no. 24, 1988, page 11837, XP001026354 ISSN: 0305-1048	14,73, 86,87, 101,102, 120-126, 129,130
Y	the whole document	88-97, 99,100
X	BILCOCK DENZIL T ET AL: "Reactions of type II restriction endonucleases with 8-base pair recognition sites" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 274, no. 51, 17 December 1999 (1999-12-17), pages 36379-36386, XP002194222 ISSN: 0021-9258	44-46, 49,50, 59-61, 64,65, 103,105, 106
A	the whole document	1-36,40, 44-102
Y	US 5 391 487 A (KAPPELMAN ET AL) 21 February 1995 (1995-02-21)	41-43
A	the whole document	1-36,40, 44-102

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	the whole document -----	1-36,40, 44-102
A	US 2003/143522 A1 (PERLER FRANCINE B ET AL) 31 July 2003 (2003-07-31) page 8, right-hand column, line 38 - page 9, right-hand column, line 2 -----	1-130
X	WO 01/07633 A (THE UNITED STATES OF AMERICA, AS REPRESENTED BY THE SECRETARY OF AGRIC) 1 February 2001 (2001-02-01)	101,102, 115,120, 129,130
Y	the whole document -----	88-97, 99,100
X	WO 91/02077 A (THE UNITED STATES OF AMERICA, REPRESENTED BY THE S) 21 February 1991 (1991-02-21)	14,73, 86,87, 120-126, 129,130
Y	the whole document -----	88-97, 99,100
X	BERGER S L: "GENE MODIFICATION WITH HAPAXOTERMINISTIC RESTRICTION ENZYMES. EASING THE WAY" METHODS IN MOLECULAR BIOLOGY, HUMANA PRESS INC., CLIFTON, NJ, US, vol. 160, 2001, pages 443-458, XP008052201 the whole document -----	115, 120-128
X	BERGER S L ET AL: "PHOENIX MUTAGENESIS: ONE-STEP REASSEMBLY OF MULTIPLY CLEAVED PLASMIDS WITH MIXTURES OF MUTANT AND WILD-TYPE FRAGMENTS" ANALYTICAL BIOCHEMISTRY, ACADEMIC PRESS, SAN DIEGO, CA, US, vol. 214, 1993, pages 571-579, XP002043107 ISSN: 0003-2697 the whole document -----	115, 120-128

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Y	WO 91/05866 A (SCHERING CORPORATION) 2 May 1991 (1991-05-02) claims 1-19	37,38
Y	WILMS B ET AL: "High-cell-density fermentation for production of L-N-carbamoylase using an expression system based on the Escherichia coli rhaBAD promoter" BIOTECHNOLOGY AND BIOENGINEERING, WILEY & SONS, HOBOKEN, NJ, US, vol. 73, no. 2, 20 April 2001 (2001-04-20), pages 95-103, XP002228440 ISSN: 0006-3592 cited in the application the whole document	37,38
Y	STUMPP T ET AL: "EIN NEUES, L-RHAMNOSE-INDUZIERBARES EXPRESSIONSSYSTEM FUER ESCHERICHIA COLI" BIOSPEKTRUM, SPEKTRUM AKADEMISCHER VERLAG, DE, vol. 6, no. 1, 2000, pages 33-36, XP009004621 ISSN: 0947-0867 the whole document	37,38
Y	EP 0 178 863 A (SCHERING CORPORATION) 23 April 1986 (1986-04-23) claims 1-13	37,38
Y	EP 0 792 934 A (COUNCIL OF SCIENTIFIC AND INDUSTRIAL RESEARCH; DEPARTMENT OF BIOTECHNO) 3 September 1997 (1997-09-03) claims 1-26	37,38
X	HARTLEY R W: "BARNASE AND BARSTAR EXPRESSION OF ITS CLONED INHIBITOR PERMITS EXPRESSION OF A CLONED RIBONUCLEASE" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 202, no. 4, 1988, pages 913-915, XP000993227 ISSN: 0022-2836 third invention the whole document	39

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	JUCOVIC MILAN ET AL: "In vivo system for the detection of low level activity barnase mutants" PROTEIN ENGINEERING, vol. 8, no. 5, 1995, pages 497-499, XP008055070 ISSN: 0269-2139 the whole document -----	39
X	CHEN M ET AL: "The roles of signal peptide and mature protein in RNase (barnase) export from Bacillus subtilis." MOLECULAR & GENERAL GENETICS : MGG. JUN 1993, vol. 239, no. 3, June 1993 (1993-06), pages 409-415, XP002353285 ISSN: 0026-8925 the whole document -----	39
A	WO 01/21817 A (VLAAMS INTERUNIVERSITAIR INSTITUUT VOOR BIOTECHNOLOGIE VZW; MUYLDERMAN) 29 March 2001 (2001-03-29) claims 1-29; figures 5a-b -----	39
A	PRIOR T I ET AL: "Barnase toxin: a new chimeric toxin composed of pseudomonas exotoxin A and barnase." CELL. 8 MAR 1991, vol. 64, no. 5, 8 March 1991 (1991-03-08), pages 1017-1023, XP002353110 ISSN: 0092-8674 the whole document -----	39
Y	WO 01/55369 A (THE SCRIPPS RESEARCH INSTITUTE; THE NEUROSCIENCES INSTITUTE; MAURO, VI) 2 August 2001 (2001-08-02) claims 1-106 ----- -/--	41-43

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	MARTINEZ-SALAS E: "INTERNAL RIBOSOME ENTRY SITE BIOLOGY AND ITS USE IN EXPRESSION VECTORS" CURRENT OPINION IN BIOTECHNOLOGY, LONDON, GB, vol. 10, no. 5, 1999, pages 458-464, XP000943666 ISSN: 0958-1669 the whole document	41-43
Y	DE 195 14 310 A1 (KLINIKUM DER ALBERT-LUDWIGS-UNIVERSITAET FREIBURG, 79106 FREIBURG, DE) 24 October 1996 (1996-10-24) claims 1-14	41-43
Y	CHAPPELL S A ET AL: "A 9nt segment of a cellular mRNA can function as an internal ribosome entry site (ires) and when present in linked multiple copies greatly enhances ires activity" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE, WASHINGTON, DC, US, vol. 97, no. 4, 15 February 2000 (2000-02-15), pages 1536-1541, XP002202271 ISSN: 0027-8424 the whole document	41-43
X	EP 1 184 462 A (SMITHKLINE BEECHAM CORPORATION; SMITHKLINE BEECHAM PLC) 6 March 2002 (2002-03-06) figure 3	103,105, 106,110, 112-114
X	DENNIS JONATHAN J ET AL: "Rapid generation of nested deletions by differential restriction digestion." BIOTECHNIQUES. AUG 2002, vol. 33, no. 2, August 2002 (2002-08), pages 310 , 312 , 314-315, XP002353098 ISSN: 0736-6205 the whole document	103,105, 106,110
A	EP 0 931 835 A (NEW ENGLAND BIOLABS, INC) 28 July 1999 (1999-07-28) claims 1-7	103-114
A	EP 0 517 111 A (NEW ENGLAND BIOLABS, INC) 9 December 1992 (1992-12-09) claims 1-6	103-114

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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X	ELLROTT KYLE P ET AL: "Restriction enzyme recognition sequence search program." BIOTECHNIQUES. DEC 2002, vol. 33, no. 6, December 2002 (2002-12), pages 1322-1326, XP002353099 ISSN: 0736-6205 the whole document -----	141
X	VINCZE TAMAS ET AL: "NEBcutter: A program to cleave DNA with restriction enzymes." NUCLEIC ACIDS RESEARCH. 1 JUL 2003, vol. 31, no. 13, 1 July 2003 (2003-07-01), pages 3688-3691, XP002353100 ISSN: 1362-4962 the whole document -----	141
A	KASARJIAN JULIE K A ET AL: "New restriction enzymes discovered from Escherichia coli clinical strains using a plasmid transformation method." NUCLEIC ACIDS RESEARCH. 1 MAR 2003, vol. 31, no. 5, 1 March 2003 (2003-03-01), page e22, XP002353105 ISSN: 1362-4962 the whole document -----	131-141
A	BOLTON B J ET AL: "Ksp632I, a novel class-IIS restriction endonuclease from Kluyvera sp. strain 632 with the asymmetric hexanucleotide recognition sequence: 5'-CTCTTC(N)1-3' 3'-GAGAAG(N)4-5'." GENE. 15 JUN 1988, vol. 66, no. 1, 15 June 1988 (1988-06-15), pages 31-43, XP002353106 ISSN: 0378-1119 the whole document -----	131-141
A	STÜCKLE E E ET AL: "Statistical analysis of nucleotide sequences." NUCLEIC ACIDS RESEARCH. 25 NOV 1990, vol. 18, no. 22, 25 November 1990 (1990-11-25), pages 6641-6647, XP008055398 ISSN: 0305-1048 the whole document -----	131-141

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Information on patent family members

International Application No
PCT/US2004/031912

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